

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of the Claims:

1. (Original) A nucleic acid sequencing method comprising:
 - providing a DNA sample containing a plurality of circular single-stranded DNA template molecules each comprising a primer annealing sequence and a target sequence;
 - forming a random array of immobilized and amplified template molecules, by
 - contacting said template molecules with an amplification primer to anneal to the primer annealing sequence thereby forming annealed primer/template complexes,
 - amplifying said template molecules by rolling-circle amplification,
 - ensuring said amplified template molecules are immobilized on a solid support by immobilizing the amplification primer before annealing the template, the primer/template complexes before amplification, or the amplified templates after amplification;
 - probing the tandem-repeated amplification product with a panel of probes under test conditions, determining for each probe whether it hybridizes to the target sequences or not under the test conditions, thereby obtaining a hybridization spectrum of the target;
 - comparing the hybridization spectrum to a hybridization spectrum for reference sequences in a reference database comprising a plurality of reference sequences, wherein the reference database is expected to contain within it one or more reference sequences for the sequence of the DNA template, thereby determining the likely location or locations of the target sequence within one or more reference sequences;
 - optionally computing the likely sequence of the target sequence and/or a difference in sequence of the target sequence compared with one or more reference sequences by comparing the actual hybridization spectrum with the expected hybridization spectrum at the location or locations.
2. (Original) A method according to claim 1 comprising computing a difference in sequence of the target sequence compared with one or more reference sequences, wherein the difference is one or more or a combination of differences selected from the group consisting of single nucleotide polymorphism, insertion, deletion, alternative splicing, an alternative transcriptional start site, alternative polyadenylation, and microsatellites.

3. (Currently Amended) A method according to claim 1 ~~or claim 2~~ wherein the panel of probes comprises probes with an effective specificity of 3 to 10 bases.
4. (Original) A method according to claim 3 wherein said effective specificity is 4 to 6 bases.
5. (Currently Amended) A method according to ~~any one of claims 1 to 4~~ claim 1 wherein the size of each target sequence and the effective specificity of the full or partial panel of probes are adjusted so that the statistical probability of hybridization of each probe to each target is between 5% and 95%.
6. (Original) A method according to claim 5 wherein said statistical probability is between 10% and 90%.
7. (Original) A method according to claim 6 wherein said statistical probability is between 25% and 75%.
8. (Original) A method according to claim 7 wherein said statistical probability is between 40% and 60%.
9. (Currently Amended) A method according to ~~any one of claims 1 to 8~~ claim 1 comprising probing with multiple panels of probes, where each probe in each panel of probes is different from each probe in each other panel of probes.
10. (Currently Amended) A method according to ~~any one of claims 1 to 9~~ claim 1 wherein the reference database is compiled from sequences of nucleic acid from the same species as the target sequence.
11. (Currently Amended) A method according to ~~any one of claims 1 to 9~~ claim 1 wherein the reference database is compiled from sequences of nucleic acid from a different species from the target sequence.
12. (Original) A method according to any one of the preceding claims comprising forming a random array of single-stranded DNA molecules, wherein
each said molecule consists of at least two tandem- repeated copies of an initial sequence,

each said molecule is immobilized on a surface at random locations with a density of between 10^3 and 10^7 per cm^2 ,

each said initial sequence represents a random fragment from an initial target DNA or RNA library comprising a mixture of single- or double-stranded RNA or DNA molecules,

said initial sequences of all said DNA molecules have approximately the same length.

13. (Original) A method according to claim 12 wherein each molecule comprises at least 1000 tandem-repeated copies of an initial sequence.

14. (Currently Amended) A method according to claim 12 ~~or claim 13~~ wherein said density is between 10^5 per cm^2 and 10^7 per cm^2 .

15. (Currently Amended) A method according to ~~any one of claims 12 to 14~~ claim 12 wherein said initial sequences have the same length within 50% CV.

16. (Original) A method according to claim 15 wherein said initial sequences have the same length within 10% CV.

17. (Original) A method according to claim 16 wherein said initial sequences have the same length within 5% CV.

18. (Currently Amended) A method according to ~~any one of claims 12 to 17~~ claim 12 wherein said initial target library is an RNA library, an mRNA library, a cDNA library, a genomic DNA library, a plasmid DNA library or a library of DNA molecules.

19. (Original) A method according to any one of the preceding claims wherein, in the panel of probes:

each probe consists of one or more oligonucleotides,

each said oligonucleotide is stabilized,

each said oligonucleotide carries a reporter moiety,

the effective specificity of each probe is between 3 and 10 bp,

the set of probes is such that at least 10% of all positions in a random or arbitrary target sequence statistically hybridize with at least one probe in the set of probes.

20. (Original) A method according to claim 19 wherein the effective specificity is between 4 and 6 bp.

21. (Currently Amended) A method according to claim 19 ~~or claim 20~~ wherein the panel of probes statistically hybridizes to at least 25% of all positions in a target sequence.
22. (Original) A method according to claim 21 wherein the panel of probes statistically hybridizes to at least 50% of all positions in a target sequence.
23. (Original) A method according to claim 22 wherein the panel of probes statistically hybridizes to at least 90% of all positions in a target sequence.
24. (Original) A method according to claim 23 wherein the panel of probes statistically hybridizes to 100% of all positions in a target sequence.
25. (Currently Amended) A method according to ~~any one of claims 19 to 24~~ claim 19 stabilised by one or more of introduction of degenerate positions, introduction of locked nucleic acid monomers, introduction of peptide nucleic acid monomers and introduction of a minor groove binder.
26. (Currently Amended) A method according to ~~any one of claims 19 to 25~~ claim 19 wherein the reporter moiety is selected from the group consisting of a fluorophor, a quencher, a dark quencher, a redox label, and a chemically reactive group which can be labeled by enzymatic or chemical means, for example a free 3'-OH for primer extension with labeled nucleotides or an amine for chemical labelling after hybridization.
27. (Original) A method according to any one of the preceding claims, wherein the hybridisation spectra are compared using a spectral search instrument comprising a field-programmable gate array (FPGA) attached to a host computer and a computer-readable memory device, wherein
- said FPGA is configured to perform spectral search,
 - said computer-readable memory device stores a reference nucleotide sequence and a set of hybridization spectra,
 - said host computer is configured to provide said FPGA with the reference nucleotide sequence and with each said hybridization spectrum,
 - said FPGA, when provided with a reference nucleotide sequence and a hybridization spectrum, writes to said computer-readable memory to store the location or locations of best matches between said hybridization spectrum and said reference nucleotide sequence.

28. (Currently Amended) A computer processor programmed to control a method of according to ~~any one of claims 1 to 27~~ claim 1.
29. (Original) A computer-readable device carrying a program for a computer processor according to claim 28.
30. (Currently Amended) A computer processor programmed to provide sequence information for a nucleic acid from performance of a method according to ~~any one of claims 1 to 27~~ claim 1.
31. (Original) A computer-readable device carrying a program for a computer processor according to claim 30.
32. (Original) A random array of single-stranded DNA molecules, wherein
each said molecule consists of at least two tandem- repeated copies of an initial sequence,
each said molecule is immobilized on a surface at random locations with a density of between 10^3 and 10^7 per cm^2 ,
each said initial sequence represents a random fragment from an initial target DNA or RNA library comprising a mixture of single- or double-stranded RNA or DNA molecules, said initial sequences of all said DNA molecules have approximately the same length.
33. (Original) A random array according to claim 32 wherein each molecule comprises at least 1000 tandem-repeated copies of an initial sequence.
34. (Currently Amended) A random array according to claim 32 ~~or claim 33~~ wherein said density is between 10^5 per cm^2 and 10^7 per cm^2 .
35. (Original) A random array according to ~~any one of claims 32 to 34~~ claim 32 wherein said initial sequences have the same length 20 within 50% CV.
36. (Original) A random array according to claim 35 wherein said initial sequences have the same length within 10% CV.
37. (Original) A random array according to claim 36 wherein said initial sequences have the same length within 5% CV.

38. (Original) A random array according to ~~any one of claims 32 to 37~~ claim 32 wherein said initial target library is an RNA library, an mRNA library, a cDNA library, a genomic DNA library, a plasmid DNA library or a library of DNA molecules.
39. (Original) A set of probes wherein
 each probe consists of one or more oligonucleotides,
 each said oligonucleotide is stabilized,
 each said oligonucleotide carries a reporter moiety,
 the effective specificity of each probe is between 3 and 10 bp,
 the set of probes is such that at least 10% of all positions in a random or arbitrary target sequence statistically hybridize with at least one probe in the set of probes.
40. (Original) A set of probes according to claim 39 wherein the effective specificity is between 4 and 6 bp.
41. (Currently Amended) A set of probes according to claim 39 ~~or claim 40~~ which statistically hybridizes to at least 25%, at least 50%, at least 90% of all positions in a target sequence.
42. (Original) A set of probes according to claim 41 which statistically hybridizes to 100% of all positions in a target sequence.
43. (Currently Amended) A set of probes according to ~~any one of claims 39 to 42~~ claim 39 stabilised by one or more of introduction of degenerate positions, introduction of locked nucleic acid monomers, introduction of peptide nucleic acid monomers and introduction of a minor groove binder.
44. (Currently Amended) A set of probes according to ~~any one of claims 39 to 43~~ claim 39 wherein the reporter moiety is selected from the group consisting of a fluorophor, a quencher, a dark quencher, a redox label, and a chemically reactive group which can be labeled by enzymatic or chemical means, for example a free 3'-OH for primer extension with labeled nucleotides or an amine for chemical labelling after hybridization.
45. (Original) A spectral search instrument comprising a field- programmable gate array (FPGA) attached to a host computer and a computer-readable memory device, wherein
 said FPGA is configured to perform spectral search,

said computer-readable memory device stores a reference nucleotide sequence and a set of hybridization spectra,
said host computer is configured to provide said FPGA with the reference nucleotide sequence and with each said hybridization spectrum,
said FPGA, when provided with a reference nucleotide sequence and a hybridization spectrum, writes to said computer-readable memory to store the location or locations of best matches between said hybridization spectrum and said reference nucleotide sequence.